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TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER**
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/678,639	HE ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31,32,34,36 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31,32,34,36 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10/3/03* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 31, 32, 34 and 36-37 are all the pending claims for this application.

2. Claims 31, 32, 34 and 36-37 are all the claims under examination.

Withdrawal of Rejections

Claim Rejections - 35 USC § 102

3. The rejection of Claims 31 and 37 under 35 U.S.C. 102(b) as being anticipated by Song et al. (J. Biol. Chem. 275:23790-23797 (2000)) is withdrawn in view of Applicants comments on pp. 5-6 of the Response of 11/1/07 inasmuch as Song does not teach that dvl-3 is overexpressed in a cancer cell.

4. The rejection of Claims 31, 32, 34 and 37 under 35 U.S.C. 102(e) as being anticipated by Alsobrook et al. (US 20030229016; published December 11, 2003; priority to 8/26/02 and earlier) is withdrawn.

Applicant's allegations on pp. 6-10 of the Response of 11/1/07 and the 1.131 Declaration of Drs. He, You, Xu and Jablons which effectively antedates the 12/2/02 filing date of Alsobrook meets and overcomes the rejection.

The provisional applications of Alsobrook have been reconsidered for their disclosure. The examiner submits that the '903 provisional application of Alsobrook is not enabling for showing inhibition (e.g., antisense (siRNA) of dvl-3 protein expression in a dvl-3 overexpressing cancer cell. Alsobrook's other provisional applications do not

mention dvl-3. Thus Alsobrook is not entitled to claim benefit to the provisional applications for the instant claimed method.

Alsobrooks' '928 application was also reconsidered. Alsobrook contemplates siRNA for inhibiting dvl-3 expression but does not specifically show that the siRNA would work in a dvl-3-overexpressing cancer cell. Thus it is the examiner's position that Alsobrook as of 12/2/02, was not enabling for the use of siRNA in a method for modulating dvl-3 expression.

Applicants' allegations' on pp. 8-9 of the Response of 11/1/07 that the 60/509,037 provisional application for the instant application can be used to predate or antedate Alsobrook's application by two months has been considered and found persuasive in part. On closer inspection, the '037 application *does not* disclose an enabling use for using a siRNA for inhibiting dvl-3 expression in an overexpressing cancer of any kind. The '037 application discloses overexpression of dvl-3 protein in some cancers (Figure 9), and that an anti-Wnt antibody caused down-regulation of dvl-3 expression in cancer cell lines (Figure 4).

The Declaration evidence alleges that prior to 12/2/02, Applicants had completed the conception of the method for using siRNA to inhibit dvl-3 expression in a dvl-3-overexpressing cancer cell, and further that just prior to 12/2/02 and until the time of the filing for the 60/491,350 provisional application (7/31/03), the inventors had diligently reduced the siRNA method invention to practice. For all of these reasons, the rejection over Alsobrook is withdrawn.

Claim Rejections - 35 USC § 103

5. The rejection of Claims 31 and 32 under 35 U.S.C. 103(a) as being unpatentable over Song et al. (J. Biol. Chem. 275:23790-23797 (2000)) in view of Engelmann et al. (Phytomedicine 9(6):489-495 (2002) Abstract) is withdrawn in view of Applicants allegations on pp. 13-15 of the Response of 11/1/07 inasmuch as Song does not teach that dvl-3 is overexpressed in a cancer cell.

6. The rejection of Claims 31 and 36 under 35 U.S.C. 103(a) as being unpatentable over Song et al. (J. Biol. Chem. 275:23790-23797 (2000)) in view of You et al. (Proc. Am. Assoc. Cancer Res. 42: 609 (2001)) as evidenced by Uematsu et al. (Oncogene 22:7218-7221 (2003)) is withdrawn in view of Applicants allegations on pp. 15-17 of the Response of 11/1/07 inasmuch as Song does not teach that dvl-3 is overexpressed in a cancer cell.

7. The rejection of Claims 31 and 36 under 35 U.S.C. 103(a) as being unpatentable over Alsobrook et al. (US 20030229016; published December 11, 2003; priority to 8/26/02 and earlier) in view of You et al. (Proc. Am. Assoc. Cancer Res. 42: 609 (2001)) as evidenced by Uematsu et al. (Oncogene 22:7218-7221 (2003)) is withdrawn. Applicants' allegations on pp. 17-18 of the Response of 11/1/07 and the 1.131 Declaration are found to be persuasive as discussed above under section 4.

Rejections Maintained

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The rejection of Claims 31 and 37 under 35 U.S.C. 103(a) as being unpatentable over Song et al. (J. Biol. Chem. 275:23790-23797 (2000); cited in the PTO 892 form of 5/1/07) in view of Bui et al. (Biochem. Biophys. Res. Comm. 239:510-516 (1997); cited in the cited in the PTO 892 form of 5/1/07) is maintained.

Applicants' allegations on pp.11-13 of the Response of 11/8/07 have been considered and are not found persuasive. Applicants allege that neither Song nor Bui disclose "an agent that inhibits Dvl-3 expression to inhibit growth of a cancer cell" nor a cancer cell "overexpressing Dvl-3 protein".

The examiner submits that Bui discloses and compares dvl-3 expression between normal and cancerous tissues in Table 1. For example, a benign breast component cell line (2.5.2a) scored as a low expresser (+) but several breast adenocarcinoma cell lines were scored as high expressers (++). Similarly, primary cultures of endothelial cell lines were low expressers (+) whereas endometrial carcinomas were high expressers (++). Further, Bui discloses that "dvl-3 is a ubiquitously expressed gene in human cells" (p. 515, Col. 2, ¶2). Finally, Bui specifically

states on p. 515, Col. 2, ¶1 that "the data in human breast tissues also raises a possibility of high dvl-3 expression in ER positive breast tumors compared to ER negative breast tumors or normal breast tissues. This is an interesting observation which implicates a role of dvl-3 in human breast cancers." Thus inasmuch as the examples of Song (Figure 6) do not disclose treating a breast cancer cell, but only normal breast cancer cells as pointed out by Applicants in their response, the examiner submits that the reference disclosures combined provide more than sufficient motivation to target dvl-3 expression in cells expressing dvl-3 much less dvl-3 over-expressing breast cancer cell lines.

Finally, Applicants urge the examiner to consider that language for "dvl-3 expression" would be interpreted by one of skill in the art as transcription or translation (p. 5 of the Response of 11/1/07) and that the means by which dvl-3 protein expression levels are lowered in the presence of apigenin as taught by Song, are not the same as inhibiting transcription or translation.

The examiner respectfully disagrees because the limitations for inhibiting "transcription" or "translation" of dvl-3 are not read into the claims. The claims are not limited as to whether an agent should contact the dvl-3 protein or dvl-3 nucleic acid. Where the specification teaches inhibiting transcription or translation at [0103] it is in the context of siRNA. Finally, Applicants are requested to identify by exact page, paragraph and line number where in the specification the effect of *any test agent* is required to inhibit expression by transcription or translation of dvl-3 as a means for inhibiting cancer

cell growth. The examiner submits that this limitation cannot be read into the claims from the specification as filed, and therefore the rejection is maintained. Otherwise, the specification teaches, very generally, the use of small molecule inhibitors [0014] which encompass apigenin of Song.

New Grounds for Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

9. Claims 31, 32, 34, 36 and 37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibiting growth of human mesothelioma cancer cell lines and a human squamous epithelial lung cancer cell line in vitro with wnt or dvl-3 siRNA, does not reasonably provide enablement for using wnt or dvl-3 siRNA to inhibit dvl-3 expression in just any cancer in order to inhibit cancer cell growth much less in vivo. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). They include the nature of the invention, the state of the prior art, the relative skill of those in

the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability of the art, the breadth of the claims, the quantity of experimentation which would be required in order to practice the invention as claimed.

Nature of the Invention/Skill in the Art

The interpretation of Claims 31, 32, 34, 36 and 37 is of record. The relative skill in the art required to practice the invention is a clinical oncologist with a background in treating oncogenic cancers with a variety of test agents including small interfering RNA.

Disclosure in the Specification

The specification teaches in Example 4 anti-Wnt antibody-induced apoptosis is associated with down-regulation of cytosolic dvl-3 levels and that apigenin downregulates expression levels; Wnt siRNA downregulates cytosolic dvl-3 levels (Example 9); apigenin destabilizes dvl-3 and reduces protein levels in mesothelioma cells (Example 10); suppression of NCI-H1703 (squamous cell lung cancer cell line) growth by the dvl-3 siRNA but no effect on A549 (squamous cell lung cancer cell line) and SW480 (a colon cancer cell line with aberrant activation in the Wnt signaling pathway due to APC mutation) by the dvl siRNA (Figure 9). The specification teaches that siRNA and apigenin both result in degradation of dvl-3. Thus, the specification discloses inhibiting two kinds of cancer cell lines, mesothelioma and squamous cell lung cancer cell line, with dvl-3 siRNA, and in the case of the A549 (squamous cell lung cancer cell line) was ineffective altogether. The specification does not support the broad scope of the claims for inhibiting any cancer cell growth whether in vitro or in vivo,

where the cell is contacted with any agent that inhibits dvl-3 expression and which results in cancer cell growth inhibition.

Field of Art/Undpredictability/Undue Experimentation

With respect to the use of antisense molecules, at the time the instant invention was filed, the art recognized significant unpredictability to equate phenotypes derived from antisense technology with phenotypes derived from true loss-of-function methods. According to Stein (Stein, C.A., Pharmacology and Therapeutics 85: 231-236, 2000):

> "[A]ntisense oligonucleotide biotechnology has entered a phase of its development in which many problems engendered by non-sequence specificity are being recognized and being actively addressed. However, in order to improve specificity of the methodology, attention must now also be aid to co-suppression of gene activity due to irrelevant cleavage." Stein further states that "[T]o the extent that this issue also is addressed, correlations between the down-regulation of a defined target and an observed biological outcome (e.g., growth suppression) *eventually* [*emphasis added*] may be possible." (page 235, Concluding remarks)

Stein clearly suggests that use of antisense oligonucleotide therapeutics are highly unpredictable due to "irrelevant cleavage" as a result of the low stringency requirements for RNAse H activity, wherein a 5-base complementary region of oligomer to target may be sufficient to elicit RNAse H activity (see Stein, abstract).

Stein also teaches (Stein, C.A., September, J. Clinical Investigation 108(5): 641-644, 2001) that:

> "serious question have arisen as to whether an observed biological effect in an antisense experiment has indeed been produce by an antisense mechanism, or whether it is due to a complex combination of non-sequence specific effects. Investigators must therefore understand how to employ antisense technology properly and should recognize its limitations" (page 641, column 1, paragraph 2). However, in many, and perhaps most of the citations in which only a single oligomer was evaluated, the results reported may represent some combination of true

> antisense effects with sequence-nonspecific and cytotoxic effects" (page 642, column 1, lines 20-25). Except under rare and strongly justified circumstances, the use of an observed biological endpoint to claim antisense efficacy is not acceptable (page 642, column 2, lines 6-10).

Stein teaches several guidelines that reflect the state of the art at the time of filing of the instant application, including:

> (a) that although computer-based approaches are being developed, it is still necessary to choose the optimal antisense oligonucleotide sequence from a panel of oligonucleotides, e.g. by mRNA "walking", (b) down-regulation of a relevant molecular target must be demonstrated, and (c) maximizing sequence specificity and minimize sequence non-specificity.

Stein teaches that only approximately one in eight (12.5%) of the putative antisense oligonucleotides tested can be shown to be active (page 642, column 1, lines 14-18). Other useful controls include:

> (i) the use of two or more oligonucleotides of different sequences that are complementary to the same target. If the observed phenotype(s) are the same or distinct from those seen using control oligonucleotides, an antisense mechanism of target downregulation is strengthened, (ii) introduction of the target gene with one or more mutations in the region complementary to the antisense oligonucleotide. Lack of antisense inhibition in this case is suggestive, particularly if the antisense oligomer is still effective when the wildtype target is forcibly over-expressed (page 642, column 1, lines 40-65).

Caplen (Caplen, N.J., August, Gene Therapy 11(16): 1241-1248, 2004) addresses the degree of unpredictability in the art when choosing a biologically effective antisense sequence, stating that "it is unclear at this time (2004) what the minimum level of homology required between the siRNA and the target to decrease gene expression is, but it has been reported that matches of as few as 11 consecutive nucleotides can affect the RNA levels of a non-targeted transcript" (page 1245, column 2). This is especially relevant in mammalian cells because mammalian cells have

nonspecific dsRNA-triggered responses primarily mediated through interferon-associated pathways that are absent in invertebrates and plants. While RNAi appears to be easy to induce, critical analysis of RNAi derived phenotypic data should not be overlooked. The validation of the RNAi effect in mammalian cells is important and that non-specific effects of RNAi need to be carefully assessed in mammalian cells (page 1245). For example, "ensuring the specificity and quantifying the efficacy of the particular siRNA or shRNA against a clinically relevant target transcript is essential in justifying its further development."

With regard to the ability of an artisan to correlate an observed antisense RNA phenotype to a predicted phenotype using targeting vectors that knock-out, gene disruption by selective ablation is the most definitive approach. Caplen teaches that the RNAi machinery can be saturated, so there will probably be a limit to the number of different genes that can be targeted in a cell at one time (page 1244, column 1). Furthermore, Caplen expresses the importance in recognizing that there is variation in the degree of inhibition mediated by different small interfering RNA sequences which may result in the production of different phenotypes. Thus, the disclosure of a phenotype in response to the expression of a single, structurally undefined antisense molecule (page 24, Example 4, Table 2, discussed below) cannot reasonably predict the phenotype obtained when the individual gene is totally disrupted.

Based on the disclosure of the specification and the prior art teachings for the general use of antisense molecules, the quantity of experimentation required to practice the invention as claimed would require 1) determining which of the infinite universe of

antisense molecules could "target" any element in the Wnt signaling pathway that effects dvl-3 much less a dvl-3 siRNA or any one of the specific antisense molecules disclosed in the specification for dvl-3, 2) modes of delivery in a whole organism such that a single gene is inhibited and the desired secondary effect (treatment leading to the amelioration of conditions associated with the expression of a target protein in a patient) is obtained. The specification as filed provides no specific guidelines in this regard. The deficiencies in the specification would constitute undue experimentation since these steps must be achieved without instructions from the specification before one is enabled to practice the claimed invention. For example, the instant specification does not appear to teach one of skill in the art which of the siRNA oligos can be used to effectively target cancer cells in vitro. Similarly, the instant application is not enabling for the use of the four oligo's *in vivo* in multicellular organisms, such as mammals, including humans.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 31 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Song et al. (J. Biol. Chem. 275:23790-23797 (2000); cited in the PTO 892 form of 5/1/07) in view of Bui et al. (Biochem. Biophys. Res. Comm. 239:510-516 (1997); cited

in the PTO 892 form of 5/1/07) further in view of Engelmann et al. (Phytomedicine 9(6):489-495 (2002) Abstract; cited in the PTO 892 form of 5/1/07).

The interpretation of Claims 31 and 32 is of record.

The method of inhibiting lung cancer cell proliferation with agents that effect Dvl-3 expression was prima facie obvious at the time of the invention over Song in view of Bui and Engelmann.

The interpretation of Song is of record and discussed supra under section 8 in further view of Bui. Song does not teach using the method of inhibiting cancer cell growth in a lung cancer cell but Bui discloses that "dvl-3 is a ubiquitously expressed gene in human cells" (p. 515, Col. 2, ¶2).

Engelmann discloses inhibiting lung cancer in vivo with apigenin and that inhibition of tumor blood vessel growth was weak but effective whereas intratumoral necrosis was elevated. The lung cancer cell line was reported to have also been sensitive to apigenin in vitro.

One skilled in the art would have been motivated and would have been reasonably assured of success in producing the method for inhibiting Dvl-3 expression in a lung cancer cell line in order to inhibit cancer cell growth based on the combined disclosures of Song, Bui and Engelmann. Song discloses the role of Dvl-3 in kinase signaling for epithelial cells such as breast cancer cells, and the success in using the kinase inhibitor, apigenin not only to block phosphorylation of the Dvl-3 substrate but to diminish the protein levels following cell contact with the agent, with the resultant effect of inhibiting cell proliferation. Bui discloses that dvl-3 is ubiquitously expressed in human

tissues and cells, and upregulated in several cancer cell lines. Because of the success achieved by Song and the evidence that apigenin had a direct or indirect effect on Dvl-3 protein levels in a normal breast cell and Bui's disclosure that dvl-3 expression levels in cells is ubiquitous and is generally upregulated in tumors, one skilled in the art would have been motivated to have applied the method of Song to inhibiting lung cancer cell growth based on Engelmann's disclosed success in inhibiting lung cancer cell proliferation both in vitro and in vivo using the same test agent as Song, namely, apigenin. One skilled in the art would have expected that epigenin would effect dvl-3 expression in a lung tumor cell based on Song because dvl-3 protein expression would have been inherent to these cancer cell lines and overexpressed based on the disclosure of Bui.

Thus, for all of the foregoing reasons, the claimed method of inhibiting lung cancer cell growth was prima facie obvious at the time of the invention over Song, Bui and Engelmann.

11. Claims 31 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Song et al. (J. Biol. Chem. 275:23790-23797 (2000); cited in the PTO 892 form of 5/1/07) in view of Bui et al. (Biochem. Biophys. Res. Comm. 239:510-516 (1997); cited in the PTO 892 form of 5/1/07) and further in view of You et al. (Proc. Am. Assoc. Cancer Res. 42: 609 (2001); cited in the PTO 892 form of 5/1/07) as evidenced by Uematsu et al. (Oncogene 22:7218-7221 (2003); cited in the PTO 892 form of 5/1/07).

The interpretation of Claims 31 and 36 is of record

The method of inhibiting mesothelioma cell proliferation with agents that effect Dvl-3 expression was prima facie obvious at the time of the invention over Song and Bui in view of You as evidenced by Uematsu.

The interpretation of Song is of record and discussed supra under section 8 in further view of Bui. Song does not teach using the method of inhibiting cancer cell growth in a mesothelioma cell but Bui discloses that "dvl-3 is a ubiquitously expressed gene in human cells" (p. 515, Col. 2, ¶2).

You (as evidenced by Uemtasu on p. 7218 (Col. 2, ¶2)) discloses that overexpression of Dvl, is a dominant event in mesothelioma, and it appears to induce tumorigenicity by a canonical Wnt signaling pathway.

One skilled in the art would have been motivated and would have been reasonably assured of success in producing the method for inhibiting Dvl-3 expression in a mesothelioma cell in order to inhibit cancer cell growth based on the combined disclosures of Song, Bui and You as evidenced by Uemtasu. Song discloses the role of Dvl-3 in kinase signaling for epithelial cells such as breast cancer cells, and the success in using the kinase inhibitor, apigenin not only to block phosphorylation of the Dvl-3 substrate but to diminish the protein levels following cell contact with the agent, with the resultant effect of inhibiting cell proliferation. Bui discloses that dvl-3 is ubiquitously expressed in human tissues and cells, and upregulated in several cancer cell lines. Because of the success achieved by Song and the evidence that apigenin had a direct or indirect effect on Dvl-3 protein levels in a normal breast cell and Bui's disclosure that dvl-3 expression levels in cells is ubiquitous and is generally upregulated in tumors, and

You discloses upregulated expression of dvl-3 in mesotheliomas, one skilled in the art would have been motivated to have applied the method of Song to inhibiting mesothelioma growth based on You using the same test agent as Song, namely, apigenin. One skilled in the art would have expected that epigenin would effect dvl-3 expression in a mesothelioma cell based on Song because one skilled in the art could have reasonably expected dvl-3 protein expression would have been inherent to these cancer cell lines, and further because You as evidenced by Uemtasu teach that dvl-3 was overexpressed in mesothelioma.

Thus, for all of the foregoing reasons, the claimed method of inhibiting mesothlioma cell growth was prima facie obvious at the time of the invention over Song, Bui, You and Uemtasu.

Conclusion

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LAB

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER